Patent Office asserts that the specification does not provide support for a method wherein "the treatment period is 3 to 6 weeks."

However, Applicants respectfully note that the Patent Office previously agreed that there was support for the language "3 to 6 weeks" (see the attached March 28, 2001 Interview Summary). Thus, Applicants continue to believe that this limitation is sufficiently described. (for example, on page 6, lines 15-19 and in TABLE II on page 10, showing valves "after 3 and 6 weeks of treatment").

For at least the above reasons, reconsideration and withdrawal of the rejection of claims 34 and 35 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Section 102/103 Rejections

The Office Action rejects claims 18, 20, 23-26 and 32-33 under 35 U.S.C. § 102(b) as anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over Toshihide et al. and over Pettersson et al.

The present invention relates to the new use of EPO for alleviating the disease activity of chronic inflammation in general and rheumatoid arthritis in particular. The disease activity of rheumatoid arthritis (RA) is for example assessed by determining grip strength, number of swollen or painful joints, morning stiffness or pain score. The examiner is of the opinion that Pettersson et al. and Toshihide et al. inherently disclose the alleviation of RA disease activity.

Pettersson et al. describe a 24-week open clinical study in which 12 patients with RA and anemia were treated with EPO. One patient discontinued treatment with EPO because of moving abroad. The results of this patient are not included in the statistical

calculations (see page 190, right column, fourth paragraph). Hence, 11 patients completed the study. Furthermore, it is disclosed on page 190, right column, first paragraph that *"Ten patients received oral iron supplementation for at least 20 out of the 24 weeks of treatment with rHuEPO."* It is clear from the patent application that (page 4, lines 6 to 15) *"Iron (free and/or bound in ferritin) deposits are known to occur in the synovia of Ra-affected patients. Synovial fluid iron levels correlate with RA activity and therefore it is thought that iron is involved in the initiation or maintenance of RA synovitis through mediating tissue damage.*

The role of iron in the pathogenesis of RA may be related to the fact that iron stimulates the production of hydroxyl radicals, which are potent agents in the destruction of cartilage, membranes and proteins." Hence, this leads to the following conclusions: (i) the steps as outlined in Pettersson et al. are not identical to the steps in the present claims (no iron supplementation) and (ii) it is clear that Pettersson came to the conclusion that *"there was no significant change in our patients' joint status or in their ESR and CRP values..."* (see page 192, left column, second paragraph), because the supplementation of free iron has a negative effect on the RA disease related symptoms.

Hence, Pettersson et al. clearly do not disclose, and certainly not inherently disclose, and moreover could not disclose the method as claimed by the present inventors.

Furthermore, because Petersson et al. do not suggest omitting the supplementation of iron, the claims are clearly inventive. The claims are therefore novel and would not have been obvious over Pettersson et al.

Toshihide et al. disclose the use of EPO during 2 or 3 weeks for increasing erythropoiesis in RA patients. However, it is disclosed that during this treatment period 800 or 1200 ml of blood was collected from said patients; this step is not performed in the presently claimed method. Hence, there is a clear difference between the present claims and the method disclosed in Toshihide et al.

Furthermore, the substantial removal of blood leads to less EPO being available for the treatment of RA disease symptoms. Hence, Applicants are of the opinion that due to the blood removal (and as a consequence: lower available EPO levels), the patients described in Toshihide et al. are not inherently treated for RA disease symptoms. If the patients in Toshihide et al. experienced improvement of RA disease symptoms (which is not disclosed) this is induced, according to applicant's opinion, by the removal of the blood, because with the removal of the blood the amount of iron is reduced and hence, as already outlined above, the RA disease symptoms are decreased. If the Toshihide document inherently disclose treatment of RA disease related symptoms this is induced by lower levels of iron.

Hence, the present claims are also inventive over Toshihide et al. There is no pointer in Toshihide et al. that EPO can be used to alleviate RA disease related symptoms and hence the claims are also inventive over Toshihide et al. The present claims are novel and would not have been obvious over Toshihide et al.

The Office Action makes a new rejection of claims 18, 20, 23-26 and 31-33 under 35 U.S.C. § 102(b) as being anticipated by Swaak et al. (Recombinant human erythropoietin (r-hu-EPO) treatment in patients with rheumatoid arthritis and anaemia of chronic disease (ACD); Clin Exp. Rhuematol page 577 (1994)).

According to 35 U.S.C. § 102(b), a person shall be entitled to a patent unless-- "the invention was patented or described in a printed publication in this or a foreign country...more than one year prior to the date of the application for patent in the United States."

Applicants have attached hereto a letter from the Managing Editor of "Clinical and Experimental Rheumatology" showing that the article "Recombinant human erythropoietin (r-hu-EPO) treatment in patients with rheumatoid arthritis and anaemia chronic disease (ACD)" by Swaak et al. was published no earlier than October 31, 1994.

The International filing date of the PCT application upon which the present application is based was filed October 26, 1995, which is less than one year from the date of publication of the Swaak et al. paper. Thus, the Swaak et al. paper is not properly prior art under 35 U.S.C. § 102(b), against the present application

For at least the above reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) and/or under 35 U.S.C. § 103(a) are respectfully requested.

Conclusion

Thus, for at least the above reasons, Applicants respectfully submit that this application is in condition for allowance. Favorable consideration and prompt allowance is earnestly solicited.

Should the Examiner believe anything further is necessary in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' representative at the telephone number listed below.

In the event this paper is not being timely filed, the Applicants respectfully petition for an appropriate extension of time. Any additional fees may be charged to Counsel's Deposit Account 01-2300, referring to client-matter number 108214-07002.

Respectfully submitted,

Robert K. Carpenter
Registration No. 34,794

Customer No. 004372
ARENT FOX KINTNER PLOTKIN & KAHN, PLLC
1050 Connecticut Avenue, N.W., Suite 400
Washington, D.C. 20036-5339
Tel: (202) 857-6000
Fax: (202) 638-4810
RKC/mzk